5. Lines 4 and 5 from the bottom of page 19 in paragraph 0057 teach " The fatty acids (PUFAs) may be present in any physiologically acceptable form including but not limited to glycerides, esters, free acids, amides, phospholipids or **salts".**

6. Line 2 of paragraph 0014, while referring to the published US Patent 5,932,545, states " ...peptide or **salt** thereof...".

The state of the art information relating to "salt solutions" as applied to the present invention:

The **Exhibit A** attached along with the **previous** response filed on July 12, 2006, contained 12 pages listing 12 examples of publicly available references in related literature describing regarding the use of **salt solutions** (including **lithium and sodium** salts) of a PUFA such as gamma-linolenic acid. The 12 examples of published literature, for easy reference by the Examiner, included:

1. "In vivo and invitro biotransformation of the **lithium salt** of gamma-linolenic acid...." by de Antueno R. Elliot M et al, in Br J cancer 1997.

2. "The effects of n-6 polyunsaturated fatty acids ...." by Jiang WG, et al in Br J Cancer, 1998.

3. "Growth inhibitory effect of **lithium** gammalinolenate...." by Ravichandran D, et al, in Eur J cancer, 1998.

4. "Effect of **lithium** gamma-linolenate....." by Ravichandran D, et al, in Br J Surg, 1998.

5. "A preliminary study on intravenous infusion of **sodium** eicosapentaenoate" by Liu Y et al, in Drug Dev Ind Pharm, 2000.

6. "Comparative anti-mitotic effects of **lithium** gamma-linolenate...." by Seegers JC, et al, Department of Physiology, University of Pretoria, South Africa.

7. "An open-label phase.....using **lithium** gammalinolenate" by Fearon KC, et al, in Anticancer Res, 1996.

8. "The spermicidal activity.....polyunsaturated fatty acids and their **sodium** salts", by Wang JZ et al, (Chinese article) in Shengzi Yu Biyun, 1987.

9. "Stimulation of afferent nerve terminals....**sodium** salts of some long-chain fatty acids", by Orbach J, and Andrews WH, in PMID 4489893 of PubMed.

10. "Lithium gamma-linolenate-induced ....", by Kinchington D, et al, in FEBS Lett, 1993.

11. "The effect of **lithium** gamma-linolenate .....", by Kairemo KJ, et al in Pancreas, 1998.

12. "Comparative anti-mitotic effects of **lithium** gamma-linolenate....", by Seegers JC, et al, Department of Physiology, University of Pretoria, South Africa.

The previous response filed on July 12, 2006, also included an **Exhibit B** which contained 5 pages of information from the commercial outfit called SIGMA-ALDRICH of St. Louis, MO, USA, from where salts of PUFAs, for example, **sodium salt** of Linoleic acid, may be commercially procured. Other examples of suppliers are known to those skilled in the art, to whom the present specification is directed.

It is clear from the foregoing discussion that the composition and the use of **salt solution** and **lithium salt solution** in the context of the present invention are not only clear from the specification as originally filed, but also abundantly found in related prior art. Since salt solutions of PUFAs (including sodium and lithium salt solutions of PUFAs) are known to those skilled in the art, applicant believes that references to lithium **salt solution** of PUFAs in the specification **as filed** are completely intelligible to one skilled in the art. The term "**mixture**" as used in the present invention is clearly taught at least in paragraphs 0046 and 0047 of the specification as originally filed. More

particularly, paragraph 0046 of the originally filed text material clearly spells out that **mixture** is **fatty acid + anti-angiogenic protein or peptide.**

Applicant submits that in view of the above discussion, the teaching and the **use/ composition** of salt or salt solution and **mixture** in the context of this invention are very clear from the specification as originally filed, and also well known in the art relating to cancer treatment, to which the present invention relates (vide: specification paragraph 0003). It is submitted that the specification is sufficient from the 35 USC 112 1st paragraph viewpoint and, the expression **"salt solution"** in the context of this invention is certainly intelligible to one skilled in the art. It is believed therefore that the 35USC 112 1st paragraph rejection of the specification is not applicable.

Rejection of claims 1-4 under 35USC 112, 2nd paragraph:

Claims 1-4 are rejected under 35 USC 112, 2nd paragraph.

The Examiner has objected to the use of the term "salt solution mixture" in claim 1 as being inappropriate. Applicant has amended claim 1 as seen in the claims-attachment, wherein the term "salt solution mixture" is **deleted**. The currently amended claim 1 includes a paragraph (b) which recites:

> (b) intra-arterially injecting into the located artery a predetermined quantity of one or more anti-angiogenic substance(s), and a salt of at least one polyunsaturated fatty acid chosen from linoleic acid, gamma-linolenic acid, dihomo-gamma-linolenic acid, arachidonic acid, alpha-linolenic acid, eicosapentaenoic acid, docosahexaenoic acid and cis-parinaric acid.

It is submitted that there is ample support in the specification for the term "**salt**" as exemplified at least in paragraphs 45, 46, 48 and 57 of the text as originally filed.

It is also submitted that eventhough currently amended claim 1 does **not** recite "mixture", there is ample support in the originally filed specification for the use of the term "**mixture**". Examples of the teaching of "mixture" in the context of this invention

may be found in the specification at least in paragraph 0046 (mixture=fatty acid+ anti angiogenic protein), paragraph 47 {..mixture of i) an anti-angiogenic protein/peptide; ii) a lithium salt solution...}, and in line 8 of paragraph 055.."delivering a chosen admixture of salts of predetermined fatty acids and predetermined anti-angiogenic substances..."

It is noted that the terminology in the currently amended claim 1 is devoid of the terms "salt solution mixture" or "solution mixture" which are considered inappropriate in claim 1 by the Examiner. Accordingly, it is believed that the 35 USC 112- 2nd paragraph rejection of claim 1 is overcome. It is submitted that dependent claims 2-4 which depend from amended claim1, satisfy the requirements of 35 USC 112- 2nd paragraph for reasons discussed above.

In light of the foregoing discussion and analysis and identification of the required supporting material in the specification, it is believed that the 35 USC 112 1st and 2nd paragraph rejections are not applicable. It is believed accordingly that the currently amended claim 1 including the dependent claims 2-4, are patentable.

It is also noted that claims 5-7 were indicated as allowed in the Office Action mailed September 30, 2005, and Applicant is keen on obtaining an allowance of the claims 5-7.

The 35 USC 112 objections and all objections having been overcome, since there are no other outstanding objections, an early notice of allowance of currently amended claim 1, and all the remaining claims including claims 2-4 and 5-7 is earnestly requested.

The undersigned may be reached at **215 661 1140** if any further minor amendments to the claim 1 language would assist in expediting the prosecution to completion.

Respectfully submitted.

Rama B Nath (Registration No 27,072) November 29, 2006

Marked-up Copy of Claims

1. **(Currently amended)** A method of inhibiting blood supply to a tumor, comprising the steps of:

   (a) locating an artery which carries major blood supply to the tumor, said artery being one that is proximate to the tumor; and

   (b) intra-arterially injecting into the located artery a predetermined quantity of one or more anti-angiogenic substance(s), [a salt solution mixture of a polyunsaturated fatty acid in the form of a salt solution] and a salt of at least one polyunsaturated fatty acid chosen from linolenic acid, gamma-linolenic acid, dihomo-gamma-linolenic acid, arachidonic acid, alpha-linolenic acid, eicosapentaenoic acid, docosahexaenoic acid and cis-parinaric acid [and one or more anti-angiogenic substance(s)].

2. **(Original)** A method as in claim 1 comprising the step of causing antiangiogenic action, wherein said polyunsaturated fatty acid is in the form of a lithium salt solution and wherein said predetermined quantity of the fatty acid is generally in a range of 0.5 mg to 50 gm.

3. **(Previously presented)** A method as in claim 1 wherein step (b) comprises intra-arterially injecting said predetermined quantity of a polyunsaturated fatty acid in the form of a lithium salt solution of a polyunsaturated fatty acid, wherein said anti-angiogenic substance is to the extent of 1 to 1000 mg/kg/ body weight, said solution

of polyunsaturated fatty acid further comprising a substance chosen from glycerides, esters, free acids, amides, phospholipids and salts.

4. **(Original)** A method as in claim 1, wherein the polyunsaturated fatty acid is in the form of a lithium salt solution of gamma-linolenic acid and eicosapentaenoic acid/docosahexaenoic acid, including a predetermined quantity of said anti-angiogenic substance chosen from: an anti-angiogenic substance naturally occurring as a protein, platelet factor-4, TNP-470, thalidomide, interleukin-12, and metalloprotease inhibitors, and a predetermined anti-cancer drug.

5. **(Original)** A method of treating a tumor and facilitating visualization of remission of the tumor responsive to treatment, comprising :

(a) locating an artery which carries a major portion of blood supply to said tumor and is adjacent to the tumor;

(b) obtaining an initial radiographic image of the tumor region;

(c) injecting into the located artery a mixture of at least

(i) an oily lymphographic agent as a carrier containing one or more of anti-angiogenic substance(s)

(ii) a lithium salt solution of at least one polyunsaturated fatty acid

chosen from linoleic acid, gamma-linolenic acid, dihomo-gamma-linolenic acid, arachidonic acid, alpha-linolenic acid, eicosapentaenoic acid, docosahexaenoic acid and cis-parinaric acid

(d) obtaining second and subsequent radiographic images of the tumor region after predetermined lapses of time; and

(e) comparing the initial radiographic image with the second and subsequent images to assess an extent of remission of the tumor.

6. (Previously presented) A method as in claim 5 wherein step (c) comprises intra-arterially injecting said mixture containing components chosen from : an anti-angiogenic substance naturally as a protein, platelet factor-4, TNP-470, thalidomide, and interleukin-12, causing anti-angiogenic action by inhibiting the blood supply to the tumor, wherein further the oily lymphographic agent acts as a carrier for said anti-angiogenic substance(s), and also for the lithium salt solution of predetermined quantities of gamma-linolenic acid, eicosapentaenoic acid and/or docosahexaenoic acid.

7. (Previously presented) A method of treating a cancerous tumor, comprising

(a) using an oily lymphographic agent as a carrier for

(i) at least one polyunsaturated fatty acid chosen from a lithium salt of at least one of linoleic acid, gamma-linolenic acid, dihomo-gamma-linolenic acid, arachidonic acid, alpha-linolenic acid, eicosapentaenoic acid, docosahexaenoic acid, and cis-parinaric acid; and,

(ii) a predetermined anti-cancer drug, and anti-angiogenic substance(s) mixed with polyunsaturated fatty acids or coupled with fatty acids; and,

(b) administering, by injecting into said cancerous tumor a predetermined quantity of the fatty acids, anti-cancer drug and predetermined anti-angiogenic substance in the oily lymphographic agent as a carrier.